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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/736,899	12/17/2003	Jeff D. Debad	4504-6	4043

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EXAMINER	
KOSSON, ROSANNE	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 12/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/736,899	DEBAD ET AL.	
	Examiner	Art Unit	
	Rosanne Kosson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24 and 57-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24 and 57-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on November 17, 2005 has been received and entered. No claims have been amended. Claims 25-36 have been canceled. No claims have been added. Accordingly, claims 1-24 and 57-59 are examined on the merits herewith.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Allowable Subject Matter

Claims 17 and 18 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16, 19-24 and 57-59 are again rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. This rejection was discussed in the previous Office action.

Applicants assert that their specification provides written description for any marker from any organism that may be extracted from any sample with nitrous acid, or

with any oxidizing acid, because the previous Office action did not provide enough evidence or reasons why the full scope of the claims is not adequately described.

In reply, all of Applicants' arguments have been considered, but they are not persuasive. As previously discussed, Applicants have disclosed only four markers that can be extracted with one oxidizing acid, nitrous acid- Streptococcal Group A antigen (a polysaccharide), and three viral proteins, surface antigens from Influenza A, Influenza B and RSV (Respiratory Syncitial Virus). The prior art shows that additional Streptococcal group antigens (polysaccharides) may be extracted with nitrous acid solutions- Groups B, C, F and G. The combination of the specification and prior art discloses that five Streptococcal markers and 3 viral markers may be extracted with nitrous acid. Thus, a huge gap remains between what has been described and what is claimed, as only eight species of a huge claimed genus have been disclosed. Also missing from the specification and from the art are teachings that a sizeable group of molecules having a particular common structure and that are markers of organisms, or that a sizeable group of molecules having certain structural features and a common function and that are markers of organisms, are extractable with nitrous acid solutions. Such teachings would allow one of skill in the art to recognize which marker molecules not disclosed in the specification would be expected to be extractable with nitrous acid solutions. Therefore, based on the specification and the prior art, one of skill in the art cannot determine which organism markers beyond those disclosed would be extracted, or would be expected to be extracted, with nitrous acid solutions.

On p. 7 of their Response, Applicants note that, ironically, on pp. 6 and 9 of the previous Office action, Examiner repeats the belief that, in response to a patient's complaint about her sore throat, two separate samplings, extractions and test would be required. This anecdotal story and Examiner's reaction to it are not found on these pages.

Applicants assert that one of skill in the art would readily recognize from the original disclosure that Applicants invented the presently claimed subject matter. In reply, as previously discussed, one of skill in the art would recognize readily that Applicants have invented a method of detecting the presence of Influenza A, Influenza B and RSV, either alone or in combination, in a biological sample, the method comprising extraction of a surface protein with a nitrous acid solution. One of skill in the art would also recognize readily that methods of detecting Streptococci in biological samples, comprising extracting group antigens with nitrous acid solutions are known in the art. One of skill in the art would find no information on the extraction of other organism markers with nitrous acid solutions, e.g., markers of HIV, Hepatitis C, *Plasmodium*, etc. Therefore, one of skill in the art would not consider that Applicants were in possession of the full scope of the invention as claimed at the time of filing. Thus, the rejection of record is maintained.

Claims 1-16, 19-24 and 57-59 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of measuring a plurality of organisms (two or more) in which the organisms are selected from the

consisting of Strep A, Strep B, Strep C, Strep F, Strep G, Influenza A, Influenza B and RSV, by measuring a surface antigen marker of each organism, does not reasonably provide enablement for a method of measuring a plurality of organisms (two or more) in which the organisms may be any two or more organisms, or a method of measuring any two or more markers, or a method of measuring any one marker that is viral or protein, or a method of measuring a streptococcal group-specific antigen and any viral marker. This rejection was discussed in the previous Office action.

Applicants assert that the claimed invention is fully enabled, because the previous Office action did not provide enough evidence or reasons why the full scope of the claims is not enabled. Applicants also assert that Examiner requires working examples for enablement and that the amount of experimentation required to enable the full scope of the claims is not undue.

In reply, all of Applicants' arguments have been considered, but they are not persuasive. The previous Office explains at length why the full scope of the claims is not enabled. All of the Wands factors have been considered and discussed, as well as the types of experimentation required by one of skill in the art, not by Applicants, to fill in the gap between the information needed and the information provided to practice the full scope of the claims.

The previous Office action discusses that a great deal of guidance is needed to establish that a nitrous acid solution can extract any marker from any organism, or any virus, because the claims recite measuring any marker from any organism as long as two or more organisms are present in a sample, or measuring any marker from any

organism if only one organism is present in the sample as long as the marker is protein or viral. But, as discussed above, the combination of the specification and the prior art discloses that five Streptococcal markers and three viral markers may be extracted with a nitrous acid solution. Eight markers is a long way from any marker, particularly as the specification and prior art do not disclose any systematic guidelines for determining which organism markers may be extracted with a nitrous acid solution, such as guidelines based on the structure and function (or other common properties) of these molecules. Because insufficient guidance is provided, one of skill in the art could not predict that a nitrous acid solution could extract any two markers or any one viral or protein marker from a sample so that one or more particular organisms may be identified.

Examiner has not required working examples to enable the scope of the claims, but has stated that more supporting information is needed because so little is provided.

Undue experimentation is required to practice the invention as claimed because of the large gap in the amount of information provided and the amount of information needed, the gap to be filled in by one of ordinary skill in the art. As noted above, because of the lack of systematic guidance, random, trial-and-error experimentation would be required to determine which organism markers could be extracted with a nitrous acid solution, particularly as the target markers may be protein, carbohydrate, lipid, nucleic acid, or simple or complex organic molecules. Applicants refer to pp. 23-26 of the specification, but these pages do not describe how to test and adjust the extraction reagents. They merely recite the concentrations of nitrous acid (0.5-10 M)

and another acid (0.1-0.5 M), preferably acetic acid, that may be used. Large concentration ranges are not especially helpful. See the third paragraph on p. 24, which also states that a matching concentration of the second acid is to be used with a particular concentration of nitrous acid. Because different concentration ranges are given for the two acids, it is not clear what a matching concentration is, or, for one specific concentration of nitrous acid, what a matching concentration of the second acid would be. Additionally, if a particular marker is extracted, one would not know in advance what form or condition the marker molecule would be in. Thus, one of skill in the art would also have to come with at least one, and possibly more, assays to detect the presence of the molecule, because, if the molecule is denatured or digested by nitrous acid, a known assay for detecting the native form may not work for the denatured form. The detection assay developed would have to work in the presence of a high concentration of nitrous acid. Thus, because of the amount of work that would have to be done by one of ordinary skill in the art to practice the full scope of the invention, given the specification and the prior art, the amount of experimentation is undue.

Applicants note that their results are surprising. Presumably, Applicants are referring to their discovery that three viral markers can be extracted with a nitrous acid solution, alone or in combination or in combination with Streptococcal group antigens, and that this discovery allows the development of new clinical assays. But, unexpected results are evidence of non-obviousness. They are not evidence of enablement.

Applicants also note that Examiner alleges, ironically, on pp. 6 and 9 of the previous Office action, that one of skill in the art would not expect a nitrous-acid-based reagent to be able to extract any two markers or any one viral marker or any protein marker. Applicants have shown that this reagent can extract a plurality of markers including protein viral markers. In reply, as discussed above and previously, the plurality of markers is a set of eight markers containing three viral markers that are proteins. A specification that discloses the extraction of these three markers is not enabling for a method of extracting any marker, any marker meaning any old marker, any known marker, any marker in general, i.e., many known markers. The same applies to any protein marker or any viral marker. These statements were clear in the previous Office action, and it is difficult to imagine that Applicants have misunderstood the rejection. Because these statements were clear in the previous Office action, Examiner's comments state the rejection and are not ironic. The rejection of record is maintained.

Claim Rejections - 35 USC § 102

Claims 1-4, 7-11, 13, 57 and 58 are again rejected under 35 U.S.C. 102(b) as being anticipated by Bogart et al., US 5,494,801. This rejection was discussed in the previous Office action.

Applicants allege that their invention is not anticipated because Bogart et al. disclose measuring one organism at a time and because the reference does not suggest that its method could be multiplexed. Applicants also allege that the reference

teaches away from using a single extraction condition for measuring multiple organisms in a sample and that conditions are fairly specific for GBS.

In reply, Bogart et al. disclose that their nitrous acid extraction technique is designed to be used with samples containing a number of organisms, such as throat swabs, sputum and vaginal swabs (see col. 2, lines 9-15). Following the extraction of a sample with a nitrous acid solution, the extract is tested for the presence of one or more Streptococcal group antigens by screening the extract against a panel of different antibodies to Streptococcal group antigens to measure two or more markers. Thus, the markers are measured in a multiplexed immunoassay format (see Example 2). The reference does not provide a literal laboratory protocol, stating step-by-step how this procedure is to be carried out. But one of ordinary skill in the art would have understood that, for each sample tested, the extract obtained in Example 1 was analyzed with the panel of antibodies disclosed in Example 2. Bogart et al. note that the extraction methods disclosed in Example 1 extract Group A, B, F and G Streptococcal antigens (see col. 12, line 65, to col. 13, line 4). Consequently, the reference does not teach away from using a single extraction condition for measuring multiple organisms, certainly not for measuring different Streptococcal antigens. As for conditions being fairly specific for GBS, the extraction conditions do permit the extraction of four different Streptococcal antigens. Thus, this feature does not render the claimed invention novel with respect to the reference. Therefore, the rejection of record is maintained.

Claims 1-4, 7, 8, 10, 11, 13 and 57 are again rejected under 35 U.S.C. 102(b) as being anticipated by Slifkin et al., J Clin Micro 12(4):541-545, 1980. This rejection was discussed in the previous Office action.

Applicants allege that their invention is not anticipated because Slifkin et al. disclose using samples containing only single isolated colonies and do not disclose measuring markers of a plurality of organisms.

In reply, as previously discussed, Slifkin et al. disclose a method of measuring two or more markers in a sample containing two or more organisms by first transferring patient throat culture samples collected on clinical swabs to blood agar plates. The plates were incubated for colony growth, and, from each plate, a beta-hemolytic colony that was not isolated from background flora was tested for the presence of one or more types of Streptococci (see p. 541, right col., end of 1st full paragraph, and p. 543, left col., last paragraph). Thus, the samples of Slifkin et al. are not pure cultures; they are mixed flora. Therefore, the rejection of record is maintained.

Applicants allege that the cited references do not disclose the claimed method as recited in claims 5, 14 and 59. As discussed above, however, these claims are rejected for lacking written description and enablement (they recite a method of measuring a marker of any virus). Applicants also allege that the cited references do not disclose a method of measuring multiple markers in a multiplexed assay format. In reply, "multiplexed assay format" is not defined in the specification and is used to mean that each sample is analyzed for the presence of multiple antigens. The cited references

disclose that the extract obtained from each sample is tested for the presence of several different Streptococcal group antigens by contacting it with several different antibodies, each one an antibody to a different group antigen. Thus, the cited art discloses mulitplexed assay formats. This claim limitation does not distinguish the claimed invention from the prior art.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is 571-272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rosanne Kosson
Examiner, Art Unit 1653

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